REMARKS

Claims 1-6 and 8-61 were pending. Claims 1, 13, 20 and 27 have been amended. Claims 28-61 have been cancelled without prejudice to later filing of a continuation application in order to simplify the issues presented. Claims 62-69 have been added. No new matter has been added.

Claims 1-5, 13-20 and 27 stand rejected as obvious over U.S. Patent No. 6,259,091 ("Eiden") in view of U.S. Patent No. 6,753,523 ("Whitehouse"). Claims 6, 8-11, 21-24 and 26 stand rejected as obvious over Eiden in view of Whitehouse and U.S. Patent No. 6,140,638 ("Tanner"). Claims 12 and 25 stand rejected as obvious over Eiden in view of Whitehouse and U.S. Patent No. 5,049,739 ("Okamoto").

Claim 1 requires an ion optical device, a collision cell disposed to receive at least a portion of a mass selected ion beam from the ion optical device, and a mass analyzer disposed to receive at least a portion of the mass selected ion beam from the collision cell. Thus, claim 1 requires the ion optical device and mass analyzer to be disposed on opposite sides, i.e., upstream and downstream, respectively, of the collision cell. Claims 13 and 27 include similar limitations.

In addition, claim 1 recites that "both the first ion optical device and the mass-to-charge ratio analyzing means operate at the same mass to charge ratio, so as substantially to minimize the formation in the collision cell of interfering ions having the said mass to charge ratio." Similarly, claim 13 recites "mass selecting ... the ion beam at the analyte mass to charge ratio;" "the mass selecting step being effective substantially to minimize the formation in the collision cell of interfering ions having the analyte mass to charge ratio;" and "mass analyzing the received ion beam at the same analyte mass to charge ratio as in the mass selecting step." Claim 27 similarly recites "the mass analyzer being configured to mass analyze the received ion beam at the same mass-to-charge ratio as the ion optical device," and "the ion optical device being configured substantially to minimize the formation in the collision cell of interfering ions having the said mass-to-charge ratio."

1. Eiden fails to teach a mass selective device upstream of a collision cell

The Examiner asserts that Eiden teaches an ion optical device which is a mass selective device. Applicant respectfully disagrees.

Firstly, the Examiner appears to have combined into an alleged single disclosure various components from a number of different embodiments of Eiden, in order to argue what is disclosed in Eiden (for example, there is no embodiment which has a collision cell 710 which also has a third aperture 40 for transmitting the ion beam into a second evacuated chamber 25). It is submitted with respect that this approach is not correct and that it has resulted in some confusion as to what is actually disclosed and what is not disclosed in Eiden. In particular, in the rejection of claim 1, the Examiner asserts that a first ion optical device is inside chamber 15. However, chamber 15 is an expansion chamber, evacuated to 0.1 to 10 Torr and having first and second apertures 20, 30 which are both grounded (col. 10, lines 28-30 and 52-53). Clearly, there is no ion optical device located in chamber 15. This is also evidenced by the fact that the Examiner has provided no reference to such a component in chamber 15.

In fact, Eiden does disclose an ion optical device inside a chamber before the collision cell; namely, lens stack 750 (fig. 7).

However, in the rejection of claim 27, the Examiner has asserted that element 750 is an ion optical device configured to be mass selective, i.e. an ion discriminating unit or mass analyzer. The lens stack 750 is not a mass selective device. The lens stack 750 is not described in detail in relation to fig. 7, so it is appropriate to consider the description of lens stack 60 of fig. 1. From this, it is clear that element 750 is merely a lens stack for focusing and directing the ion beam, and no more (col. 8, lines 35-45).

In fact, Eiden itself clearly distinguishes between components that are mass selective and components that are not. Eiden notes that "Upon exiting the lens stack, the ion beam is directed into the ion discriminating unit" (col. 8 lines 59-60). Thus, it is clear that the lens stack 750 is not an ion discriminating unit, i.e., it is not mass selective device.

In col. 8, lines 49-55, Eiden lists a number of devices which *may* be configured to operate as ion discriminating units/mass analyzers, and this list includes a lens stack. However, that does not mean that all lens stacks are necessarily mass analyzers/mass selective. Although lens stack 750 is an ion optical device, it is not a mass selective device. The lens stack 750 is used to guide and transfer the ions onwards through the system, not to separate or select them according to their m/z values. The undersigned has reviewed the other portions of Eiden identified by the

Examiner, and finds nothing that would indicate the presence in Eiden of a mass selective device upstream of a collision cell.

The Examiner is directed to Applicant's earlier reply to the Office Action of June 18, 2003, filed on September 18, 2003, in which this issue was discussed in detail. Those arguments were accepted by the Examiner, so Applicant trusts that, in view of the above and previous arguments, the Examiner's objection has been overcome.

2. Whitehouse fails to teach or suggest mass analyzing a received ion beam downstream from a collision cell at the same mass-to-charge ratio as the ion optical device upstream of the collision cell

The Examiner acknowledges that Eiden does not teach a mass analyzing means operating at the same mass-to-charge ratio as an ion optical device (disregarding for the moment the fact that the ion optical device in Eiden has been shown above not to be mass selective in any way). The Examiner has therefore turned to Whitehouse for relevant teaching or suggestion.

a. Multiple line segments

The Examiner argues that Whitehouse "teaches that multiple line segments of multiple ion guides/multipoles being operated independently of one another". However, individual operation of the segments of a multipole does not teach or suggest the operation of an ion optical device and a mass analyzer at the same m/z ratio. It merely teaches that the individual segments in the same multipole may be operated independently of each other.

Thus, independent operation of Whitehouse's segments does not teach or suggest the claimed invention.

b. Multiple ion guides to narrow the range

The Examiner argues that Whitehouse teaches "multiple ion guides/multipoles being used in m/z selection in order to narrow the range of m/z values entering the TOF pulsing region in order to obtain a spectrum of only those ions of interest".

Although Whitehouse does teach narrowing the m/z range of ions entering the TOF pulsing region, this is no more than the use of a bandpass transmission device, which is entirely

conventional. It is used because the mass analyzer is a TOF analyzer and narrowing the range of m/z values passing through the system may help to improve the duty cycle, detector response and detector lifetime in the TOF analyzer, by reducing the pulse width of the ions passing into the analyzer (col. 22, lines 40-67).

However, narrowing the m/z range for ions passing into a TOF analyzer is not the same thing as operating mass selective devices either side of a collision cell at the same m/z ratio. In short, the use of a bandpass transmission before a mass analyzer does not teach or suggest the claimed invention.

c. Obviousness argument

In his rejections of independent mass spectrometer claims 1 and 27, and independent method claim 13, the Examiner asserts that it would have been obvious to have the analyzing means operate at the same mass to charge ratio in order to narrow the range of m/z values entering TOF pulsing region in order to obtain a spectrum of only those ions of interest. That is, the Examiner is arguing that it would be obvious for the skilled person to modify the fig. 7 embodiment of Eiden with teaching or suggestion from Whitehouse and thereby to arrive at the claimed invention. It is submitted with respect that this is not the case.

<u>i) Eiden and Whitehouse lie in different mass spectrometry fields</u>

Eiden lies in the field of plasma/elemental mass spectrometry, which is used to study the trace concentrations of atomic/elemental ions (col. 8, lines 24-32 and col. 15, lines 16-18).

Whitehouse states that his invention lies in the field of mass spectrometric analysis of chemical species (col. 1, lines 14-15); that is, organic mass spectrometry, analyzing the composition/structure of large, molecular ions. The ion source used in figs. 1-7, on which the Examiner has based his objections, is an electrospray ion source, which is an organic mass spectrometry ion source. Whitehouse does not refer to elemental analysis at all. He does not teach the application of his apparatus to elemental analysis, nor does he give any reasons why his apparatus might be of use with a plasma ion source.

While, broadly, Whitehouse and Eiden lie in the general field of mass spectrometry, the examiner will recognize that plasma/elemental mass spectrometry and organic mass

spectrometry are two very separate technical disciplines, used for distinct purposes and entailing different technical considerations, and that practitioners in one are by no means experts in the other. In fact, as will be discussed in more detail below, there are a number of incompatibilities between elemental and organic mass spectrometry, which divide the disciplines further. Accordingly, the skilled person in plasma mass spectrometry is not the same person as the skilled person in organic mass spectrometry.

The claimed invention requires a plasma ion source. Therefore, the claimed invention lies in the field of plasma/elemental mass spectrometry.

So, in order for the claimed invention to be obvious on the basis of Eiden in combination with Whitehouse, the skilled person in plasma/elemental mass spectrometry would need to find a) specific teaching in Whitehouse of using a mass selective device upstream of a collision cell and operating it at the same m/z as a mass analyzer downstream of the collision cell (which is not taught by Eiden), and b) motivation actually to take this teaching from the organic mass spectrometer arrangement of Whitehouse and to substitute it into the elemental mass spectrometer arrangement disclosed in fig. 7 of Eiden.

ii) The skilled person would be prejudiced against trying to combine teaching from Whitehouse with Eiden's arrangement

Organic mass spectrometry generally deals with high mass molecules and uses sectors or quadrupoles to guide ions through the system. Elemental mass spectrometry generally deals with low mass, atomic ions. Quadrupoles exhibit reduced confinement at lower ion masses. Accordingly, the skilled person in elemental mass spectrometry would not want to add further quadrupoles to his system, so would not readily consider using the (segmented) multipoles taught in Whitehouse's organic mass spectrometry arrangement, without specific motivation.

The skilled person would be confronted by a number of other obstacles which would prevent him from considering combining the teaching from an organic mass spectrometry arrangement with an elemental mass spectrometry apparatus: it would be expensive; it would increase the complexity of the apparatus; there would be no problem to be solved in the mind of the skilled person by making such a combination, in particular since Whitehouse is concerned with analyzing molecular structures, not quantifying trace elemental concentrations.

iii) Eiden and Whitehouse are concerned with different technical problems

Whitehouse uses an ion guide in a mass filtering mode to select a range of m/z ions to send into the TOF analyzer, for the conventional purpose of reducing the duty cycle of the TOF analyzer. This is not an issue for elemental analysis, since the mass range from an ICP ion source is small (up to ~300 Daltons). From electrospray ion sources, very high-mass molecular ions can be formed (many thousands of Daltons). For these to pass through a TOF flight tube and arrive at the detector (before the next pulse of ions is sent on its way) takes a considerable amount of time, so that the time between pulses needs to be relatively long and the duty cycle correspondingly high. For situations where detection of the highest mass ions is not desired, Whitehouse teaches gating them out so as to improve the duty cycle. Such considerations are not necessary in elemental analysis, so the skilled person would have no motivation to use a first mass filtering stage in an elemental mass spectrometer for the reasons Whitehouse provides.

iv) Neither Eiden nor Whitehouse discloses the problem addressed by the claimed invention

Neither Eiden nor Whitehouse teaches or even suggests the problem recognized by the present inventor. Eiden discusses "a need for a method of selectively eliminating carrier gas ions and/or a portion or all matrix ions without eliminating or neutralizing the analyte ions" (col. 3, lines 49-51). This is addressed in Eiden by directing the ion beam into a collision cell containing a selectively reactive gas, leaving an ion beam with a greater fraction of analyte ions to total ions (col. 4, lines 34-54).

However, the above use of a collision cell is acknowledged and discussed in the introduction/background of the invention section of the present application. Accordingly, at the priority date of the present invention, the skilled person can be said to have been faced with no more than the very general problem of wanting to improve the plasma ion source/elemental mass spectrometer arrangement disclosed in fig. 7 of Eiden. As such, he would have no reason to attempt to combine the teaching of Whitehouse with Eiden, for the reasons set out in detail in the above sections.

The invention claimed in the present application relates to residual problems which apply to mass spectrometers, in light of Eiden. In particular, Eiden does not address the problems of the formation of new artifact ions and re-formation of dissociated artifact ions in the collision cell, and their passing on through the system to subsequent detection, thereby interfering with proper detection of analyte ions of interest. There is also no discussion in Whitehouse of the problem of the formation of unwanted molecular ions within the collision cell.

v) Summary

With no recognition of the problem to be solved in Whitehouse or Eiden, there would be no motivation for the skilled person to want or try to modify Eiden's arrangement.

With no teaching of a common problem in Whitehouse and Eiden or that Whitehouse could be applied to elemental mass spectrometry arrangements, the skilled person would be prejudiced against trying to combine teaching from Whitehouse with Eiden's arrangement.

Even if the skilled person did try to make such a combination, there is no reason to choose any one particular set of features from Whitehouse over another set of features, since there would be no perceived advantage associated with any of them.

Without actual teaching in Whitehouse or Eiden of the problem discussed in the present application, it would not have been obvious to the skilled person to modify Eiden in view of Whitehouse and arrive at the claimed invention.

The recognition of the problem and, of course, its solution are neither disclosed nor suggested in any of the prior art relied upon by the Examiner. It is only this information, provided by the present inventor, which leads to an understanding of how the claimed plasma ion source mass spectrometer apparatus and method may be used beneficially in elemental mass spectrometry. The Examiner is reminded about the dangers of performing an ex post facto, or hindsight, analysis of the prior art now before him when considering this matter (given the fact that the prior art has come to light with knowledge of the invention which has been made).

3. Tanner and Okamoto

Tanner teaches a system in which ions pass into a collision cell 41 that includes a quadrupole 34 and then into a mass analyzer 66. However, the quadrupole 34 merely acts as a pass band, rather than operating at the same m/z ratio as the mass analyzer 66.

Okamoto teaches a collision cell 120 followed by a mass analyzer 160.

Thus, neither Tanner nor Okamoto teach or suggest operating mass selective stages on either side of a collision cell and at the same m/z ratio.

Since none of Eiden, Whitehouse, Tanner or Okamoto teaches or suggests a plasma ion source mass spectrometer with mass selective stages operating on either side of a collision cell at the same m/z ratio, so as to minimize the formation in the collision cell of interfering ions having that m/z ratio, the obviousness rejection should be withdrawn.

For these reasons at least, independent apparatus claims 1 and 27 and method claim 13 are novel and non-obvious in view of the cited prior art disclosures, as are the remaining claims by way of their dependencies on the independent claims.

Enclosed is a check for $450 for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: 9/6/05

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